

**Neuromyasthenia  
and Chronic Fatigue Syndrome (CFS)  
in Northern Nevada/California:  
A Ten-Year Follow-Up of an Outbreak**

Paula S. Strickland, PhD, MPH

Paul H. Levine, MD

Daniel L. Peterson, MD

Karen O'Brien, BS

Thomas Fears, PhD

---

Paula S. Strickland is a former graduate student at George Washington University, School of Public Health and Health Services, Washington, DC.

Paul H. Levine is affiliated with the Viral Epidemiology Branch, National Cancer Institute, Bethesda, MD and George Washington University, School of Public Health and Health Services, Washington, DC.

Daniel L. Petersen is Internal Medicine Physician, and Karen O'Brien is Technician, Sierra Internal Medicine Associates, Incline Village, NV.

Thomas Fears is Statistician, National Cancer Institute, Bethesda, MD.

Address correspondence to: Paul H. Levine, MD, George Washington University, School of Public Health and Health Services, Washington, DC 20037 (E-mail: [zpl@cu.nih.gov](mailto:zpl@cu.nih.gov)).

The authors are very grateful to George Reed, PhD, for his assistance in data analysis, and Deborah Pilkington for assistance in reviewing charts.

**ABSTRACT.** In 1984-87, an outbreak of debilitating fatigue was reported by two physicians in the private practice of internal medicine in Incline Village, Nevada. Follow-up questionnaires were sent in 1995 to the 259 patients in this outbreak. The results were analyzed to determine how many patients met the latest Centers for Disease Control and Prevention (CDC) case definition for Chronic Fatigue Syndrome (CFS), Idiopathic Chronic Fatigue (ICF), or Prolonged Fatigue (PF). Data were analyzed separately for those living in the Lake Tahoe area and those referred from other locales. Of those returning questionnaires (123/259), 41% met the CDC case definition for CFS, 56% met the criteria for inclusion in the subgroup ICF, and 3% experienced PF. In the population-based Lake Tahoe group, symptomatic women were more likely to have CFS than ICF whereas symptomatic men were likely to fit ICF criteria. Also in this group, full recovery was reported more often among Lake Tahoe participants classified as having ICF (43%) than participants classified as having CFS (15%). [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-342-9678. E-mail address: <getinfo@haworthpressinc.com> Website: <<http://www.HaworthPress.com>> © 2001 by The Haworth Press, Inc. All rights reserved.]

**KEYWORDS.** Chronic fatigue syndrome, Nevada/California, neuro-myasthenia, idiopathic chronic fatigue

## INTRODUCTION

In 1984, two internal medicine practitioners noted an apparent outbreak of fatiguing illness in Northern Nevada/California, which subsequently became the subject of several reports (1-4). Although often referred to as an outbreak of chronic fatigue syndrome (CFS), most of the studies which evaluated 259 patients in this cluster between 1984 and 1987 were carried out prior to the first published CFS working definition in 1988 (5), and it has not been clear what proportion of the patients who suffered from the fatiguing illness actually had CFS. In a ten-year follow-up to the study of Buchwald et al. (3), investigators involved with the Incline Village private practice prepared a questionnaire that was mailed in March 1995 to the 259 patients included in this report.

The questionnaire was initially designed to identify CFS patients based on the case definition described by Holmes et al. in 1988 (5). However, since this case definition does not provide a strategy for subgrouping cases of chronic fatigue which are not CFS, the CFS definition and chronic fatigue subgroups described by Fukuda et al. in 1994 (6) were used in this report. Utilizing the questionnaire data our study had four objectives: first, to summarize the ques-

tionnaire data using descriptive information in order to determine what proportion of the affected patients in the Northern Nevada/California cluster met the latest case definition of CFS (6); second, to determine what proportion met the criteria of the subgrouping described by Fukuda et al. (6); third, to determine what proportion of the patients have recovered from their illness after approximately ten years, and fourth, to determine if our earlier data suggesting a relationship between this outbreak and the subsequent increased incidence of brain tumors and non-Hodgkin's lymphoma (7) would be confirmed in this cohort.

## METHODS

### Definitions

The CFS definitions and subgroups of chronic fatigue used to categorize participants were based on the categories described by Fukuda et al. (6).

*Chronic Fatigue Syndrome:* Participants were classified as having CFS if they experienced severe fatigue that persisted or relapsed for six months or more, which was of new or definite onset; was not substantially alleviated by rest, and resulted in substantial reduction in activities. They also had to have four or more CFS associated symptoms (impaired memory or concentration, sore throat, tender cervical or axillary lymph nodes, muscle pain, multi-joint pain, new headaches, unrefreshing sleep, and postexertional malaise). Finally, their illness could not be attributed to any of a group of specific organic or psychiatric conditions known to be associated with fatigue.

*Idiopathic Chronic Fatigue:* Participants were classified as having Idiopathic Chronic Fatigue (ICF) if they experienced significant fatigue which persisted for six months or longer, but the severity of fatigue or the symptoms associated with fatigue did not meet the CFS definition.

*Prolonged Fatigue:* Participants were classified as having Prolonged Fatigue (PF) if they experienced fatigue that was severe enough to seek medical attention, but the duration of the fatigue was less than six months.

Patients were also characterized geographically to distinguish those in the proximate area of the outbreak versus those subsequently referred because of the interest of the physicians in chronic fatigue. The "*Tahoe group*" is defined as those persons who were non-referral patients and residents of the Lake Tahoe/Incline Village areas at the time of initial diagnosis.

### Questionnaire

A 30 question follow-up questionnaire was developed by the physicians and investigators involved in the initial study of chronic fatigue in Incline Village for a ten-year follow-up of the patients seen in 1984-87. In March 1995,

the self-administered questionnaire was sent to the 259 study patients reported by Buchwald et al. (3). Questions dealt with the onset and duration of fatigue, past illness and current illnesses, and all of the symptoms required by the original CFS working case definition described by Holmes et al. in 1988 (5). The questionnaire also included demographic questions (e.g., date of birth, sex, residence, and occupation) and asked about the treatment used by participants for their illness. Additionally, the questionnaire asked permission to review the participants' medical records.

*Fatigue Severity at Its Worst:* Participants were asked to describe their illness at its worst. The choices ranged from bedridden to able to carry out normal activities without fatigue. Participants were categorized into four groups based on fatigue severity. Persons who indicated that they could only work part-time or less at their work or family responsibilities were considered to have severe fatigue and included in Group 1. Group 2 consisted of participants who indicated they were able to conduct normal activities but were easily fatigued. Group 3 included those who were able to carry out normal activities with minimal fatigue, and Group 4 persons were those able to carry out normal activities without fatigue.

*Fatigue Alleviation:* Participants were asked to indicate if their fatigue was helped, lessened, or completely relieved by rest. Participants who indicated that their fatigue did not go away after rest were considered to have met the CFS criterion for fatigue that is not resolved with bed rest.

*CFS-Associated Symptoms:* Participants were asked to indicate the severity and frequency of 82 symptoms using a scale from 0 to 6 (0 = no symptom, 6 = severe and frequent). Participants were also asked to indicate whether their symptoms were a problem prior to the onset of the fatiguing illness, upon onset of the illness, or recently. The CFS-associated symptoms included muscle ache, sore throat, headache, aching joints, painful swollen cervical or axillary lymph nodes, sleep disorder (difficulty falling asleep or staying asleep or unrestful sleep), and cognitive disorder (forgetful or difficulty concentrating). Post-exertion malaise was also assessed. Participants were asked to indicate whether they felt incapacitated during or after exertion, in either situations, or neither. Symptoms not usually associated with CFS were included as "controls." Patients who had an organic or psychiatric illness that could account for their fatiguing illness were excluded.

*Recovery:* Recovery from illness was first determined by the patients' response to the question "Have you fully recovered, without having any relapse." Patients were then asked "Are you still experiencing unusual fatigue that interferes with your life in some important way?" and there were questions that asked about recovery, relapse, and range of normal activity.

*Statistical Analyses:* All of the questionnaire data were entered into a computerized database (Works 3.0 database management system software), StatXact

and EpiInfo (version 6) software were used to perform descriptive and comparative statistics. Standard contingency table methods, e.g., Chi-square and Fisher exact tests, were used to test differences in proportions. All tests are two sided and only P values < 0.05 were considered significant.

## RESULTS

Of the 259 questionnaires mailed, 123 patients returned their questionnaires, 43 questionnaires were returned due to incorrect addresses, 3 patients had died, and 90 patients did not return their questionnaires. The participant response rate was 58% (123/(259-43-3)). The participants' mean age was 49, and 64% of them were females.

### *Chronic Fatigue Classification*

Forty-one percent (50/123) of the participants met the latest case definition for chronic fatigue syndrome (see Table 1) and 56% (69/123) had ICF.

### *CFS-Associated Symptoms*

The frequency with which participants in each fatigue category reported symptoms and signs listed in the 1994 CFS case definition was determined (see Table 2). At least 70% of the participants reported experiencing the CFS-associated symptoms. The least reported symptom was sore throat, which was reported by 2% of the CFS patients, by 1% of those with ICF, and by none of the PF participants. For the ten symptoms evaluated in the case definition, the incidence of symptoms was highest for CFS participants. Cognitive and sleep disorders were particularly common and were experienced by 98% of the CFS participants.

TABLE 1. Characteristics of participants

Characteristic		CFS No. (%)	ICF No. (%)	PF No. (%)	Total No. (%)
Gender	Female	37 (74)	38 (55)	4 (100)	79 (64)
	Male	13 (26)	31 (45)	0	44 (36)
	Total	50 (100)	69 (100)	4 (100)	123 (100)
Age*	Mean	47 ± 10.4	51 ± 11.8	49 ± 4.2	49 ± 11.2

\*Age-based on date of the questionnaire in 1995

TABLE 2. Comparison of reported CFS associated symptoms

Symptoms	CFS	ICF	PF
	(n = 50) No. (%)	(n = 69) No. (%)	(n = 4) No. (%)
Fatigue ( $\geq 6$ months)	50 (100)	69 (100)	0 (0)
Normal activity reduced by $\geq 50\%$	50 (100)	28 (41)	2 (50)
Fatigue not relieved by rest	50 (100)	27 (39)	1 (25)
Muscle ache	46 (92)	40 (58)	2 (50)
Post exertion fatigue	35 (70)	20 (29)	1 (25)
Sore throat	1 (2)	1 (1)	0 (0)
Headaches	39 (78)	39 (57)	2 (50)
Joint aches	40 (80)	33 (48)	1 (25)
Tender lymph nodes	43 (86)	36 (52)	4 (100)
Sleep disorder	49 (98)	58 (84)	3 (75)
Cognitive disorder	49 (98)	24 (35)	3 (75)

### *Groups Affected by the Fatiguing Illness*

Participants ranged in age from 21 to 88; the largest category of patients were females living in the Lake Tahoe area, most of them meeting the criteria for CFS (see Table 3). The largest number of participants suffering from the fatiguing illness was between the age of 45-54. In both the Tahoe and non-Tahoe areas, the smaller number of affected participants was in the 55 and over age group.

Most of the participants (80/123) were from the Lake Tahoe area. Among those from the Tahoe area, females were more likely to have CFS than ICF (26 vs. 24) whereas males were more likely to have ICF (8 vs. 18). Also, CFS was the most common diagnosis in Tahoe patients aged 20-44 (16/27 or 59%) while in patients over age 45 only 18/53 (34%) had this diagnosis ( $p = 0.07$ ).

### *Recovery*

Among the 123 participants, 34 indicated they have recovered. Recovery paralleled the mildness of the disorder: recovery was reported by 2 of the 4 PF participants, 25 of the 69 ICF patients (36%), and 7 of 50 CFS patients (14%). There is a significant difference between the proportion of CFS and ICF participants who recovered ( $p = 0.01$ ). Participants in the Tahoe area had a higher

TABLE 3. Affected participants in the Tahoe and non-Tahoe area stratified by gender and age

Location		Gender		Age		
Category		Females	Males	20-44	45-54	≥55
		No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Tahoe (n = 80)	CFS	26 (48)	8 (31)	16 (59)	11 (34)	7 (33)
	ICF	24 (44)	18 (69)	10 (37)	18 (56)	14 (67)
	PF	4 (7)	0	1 (4)	3 (9)	0
	Total	54 (100)	26 (100)	27 (100)	32 (100)	21 (100)
Non-Tahoe (n = 43)	CFS	11 (44)	5 (28)	4 (29)	7 (39)	5 (45)
	ICF	14 (56)	13 (72)	10 (71)	11 (61)	6 (55)
	PF	0	0	0	0	0
	Total	25 (100)	18 (100)	14 (100)	18 (100)	11 (100)

rate of recovery (31%) than participants in the non-Tahoe area (21%) (Table 4) which was apparent for all groups, especially ICF (43% versus 26%,  $p = 0.05$ ).

Since patients outside of the Tahoe area were most likely referred to the Incline Village private practice, we focused on the Tahoe area participants to reduce the possible impact of referral bias. Recovery rates by fatigue status and sex are given in Table 5 for Tahoe participants.

The recovery rate from CFS (15%) was significantly less than the recovery rate from ICF (43%),  $p = 0.01$ . Overall the recovery rate of Tahoe participants was 30%. Among CFS patients, 19% of the females recovered while none of the eight males reported recovery ( $p = 0.31$ ). However, among ICF patients, males reported better recovery (61%) than females (29%),  $p = 0.06$ .

We evaluated the participants' response to the question addressing the degree with which their illness interfered with normal activity. Reviewing the patients' statement of activity as classified in Table 5, we considered those stating that they had normal activity with no or minor symptoms as normal, while those who could only maintain normal activity with effort or needed some assistance were considered partially disabled. Patients who required significant assistance or considered themselves disabled were considered as disabled.

ICF patients again had a higher recovery rate with 28/42 patients returning to normal or near-normal activity as opposed to 3/34 CFS patients. There was no gender difference in recovery from CFS (2/26 for women and 1/8 for men) or from ICF (16/24 for women and 12/18 for men).

TABLE 4. Reported recovery among Tahoe and non-Tahoe participants

	CFS	ICF	PF	Total
Location	No. (%)	No. (%)	No. (%)	No. (%)
Tahoe	5/34 (15)	18/42 (43)	2/4 (50)	25/80 (31)
Non-Tahoe	2/16 (13)	7/27 (26)	N/A*	9/43 (21)
Total	7/50 (14)	25/69 (36)	2/4 (50)	34/123 (28)

\*N/A—Not applicable, all of the PF participants were from the Tahoe area.

### *Association of Fatigue and Cancer in the Tahoe Group*

Thirteen patients with fatigue also reported a history of cancer. Five of these stated their cancer occurred prior to the onset of fatigue and 8 reported malignancies occurring subsequent to the onset of fatigue. Two of the patients had two tumors subsequent to their acute illness (a transitional cell carcinoma of the bladder and basal cell carcinoma in one and a thyroid carcinoma and fatal brain tumor in the second). The other lesions identified in patients subsequent to the onset of fatigue included a B-cell lymphoma (Stage IIIA), an adenocystic carcinoma of the breast, and a melanoma.

## **DISCUSSION**

Although clusters of fatiguing illnesses have been described since 1934 (8-11), the reported outbreak in northern Nevada-California has attracted the greatest interest (1) and has been cited as evidence that CFS can occur in clusters. The report by Buchwald et al. described the epidemiology of this disorder, including reported "epidemic" and "endemic" cases, and documented the fatiguing illness in 259 patients (3). A similar smaller cohort of "epidemic neuromyasthenia" has also been studied in West Otago, New Zealand (12). In both clusters, the case definition for CFS had not yet been developed but it was possible to retrospectively evaluate the cases according to the new classification of Fukuda et al. (6), which includes several subcategories of fatigue—CFS, ICF and PF. Each cohort provided an opportunity to determine the natural history of the illness. A major advantage of the follow-up study in these clusters is that the patients were all evaluated by a single small group of physicians who had ten years to rule out other illnesses and clarify the diagnosis.

Although questionnaires were sent to all 259 patients in the initial report, our analysis concentrated on those living in the Lake Tahoe area because most of them had been followed in the practice of the internists first describing the outbreak and referral bias was minimized. The overall response rate of 57%



TABLE 5. Range of activity among participants in the Tahoe area

Category	Range of Responses											Total		
	NORMAL					PARTIALLY DISABLED					DISABLED			
	Normal, no symptoms	Normal, w/minor symptoms	Normal w/ effort, some symptoms	Unable to carry on normal activities	Occasional assistance needed	Much assistance required	Disabled, special assistance needed	Severely disabled						
Status	1	2	3	4	5	6	7	8						
Gender*	M	F	M	F	M	F	M	F	M	F	M	F		
CFS	0	1	1	1	4	9	1	5	2	6	0	0	0	34
ICF	9	3	3	3	4	5	1	3	1	0	0	0	0	42
PF	0	2	0	0	0	0	0	0	0	1	0	0	0	4
Total	9	6	4	4	8	14	2	8	3	7	0	0	0	80

M = males F = females

M = males F = females

(123/259) is good for a mail survey (13, 14). Several phone calls were made to non-responders. It is of interest that 41% (50/123) of the participants fulfilled the 1994 case definition for CFS, with 43% of the Lake Tahoe area participants apparently having CFS.

The demographics of our population were comparable to those reported in the literature. CFS has been reported to occur primarily in females (15-17) and 74% of our CFS patients were female (68% of those in the Lake Tahoe group). Of interest was the comparison of gender differences in CFS and ICF. The tendency for males to have more ICF than CFS (18 vs. 8) as opposed to females (24 vs. 26) resemble the pattern reported in the West Otago, New Zealand cluster, which noted a female predominance in those meeting the CDC case definition and a predominance of males in patients diagnosed as having ICF or PF (12). There are several possible explanations for this finding, which could include the possible autoimmune nature of CFS and the greater susceptibility of women to autoimmune disorders. Gender differences in immune function possibly relating to CFS have recently been described (18).

The symptoms that were most prominent in our study population were sleep disorder, cognitive disorder, and muscle ache. The least reported symptom was sore throat, but this may represent recall bias.

An important focus of this study, the long-term outcome, was of interest especially when compared with the New Zealand outbreak. In this ten-year follow-up study, evaluation of the Lake Tahoe area cohort showed that 31% returned to normal activity compared with 70% in the New Zealand group. We have already reviewed the heterogeneity of "epidemic neuromyasthenia" from the neurologic viewpoint (11) and have noted that clusters of fatiguing illness can be precipitated by different agents. The somewhat higher recovery in the West Otago patients could possibly be due to different precipitating organisms (a high percentage of these patients had predominant gastrointestinal symptoms, presumed by their physician to be due to giardiasis (Snow, personal communication), whereas only upper respiratory tract symptoms were noted in the northern Nevada/California group) and/or differences in altitude, which is significantly higher in Lake Tahoe.

Regarding the possible association between CFS and cancer, our data do not have sufficient numbers of patients to reach a conclusion. But it is of interest that our small study group had patients with Non-Hodgkin's lymphoma and brain cancer, both noted to be in excess in our earlier study of cancer following the reported outbreak (7). Also, the observation of patients with multiple primary tumors suggests the possibility of cancer being an outcome of CFS in those patients with immune dysfunction.

In summary, this study adds to our perspective on the widely reported northern Nevada-California cluster by showing the high prevalence of CFS cases in this cohort, and the recovery rate of the CFS cases in a study that is more population-based than cases identified by tertiary care centers.

## REFERENCES

1. Barnes DM. Mystery disease at Lake Tahoe challenges virologists and clinicians. *Science* 1986;234:541-2.
2. Daugherty SA, Henry BE, Peterson DL, Swarts RL, Bastien S, Thomas RS. Chronic fatigue syndrome in northern Nevada. *Rev Infect Dis* 1991;13 (suppl 1): S39-44.
3. Buchwald D, Cheney PR, Peterson DL, et al. A chronic illness characterized by fatigue, neurologic and immunologic disorders, and active human herpesvirus type 6 infection. *Ann Intern Med* 1992;116:103-13.
4. Levine PH, Jacobson S, Pocinki AG, et al. Clinical, epidemiologic and virologic studies in four clusters of the chronic fatigue syndrome. *Arch Intern Med* 1992; 152:1611-6.
5. Holmes GP, Kaplan JE, Gantz NM, et al. Chronic fatigue syndrome: a working case definition. *Ann Intern Med* 1988;108:387-9.
6. Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International chronic fatigue syndrome study group. *Ann Intern Med* 1994;121:953-9.
7. Levine PH, Fears TR, Cummings P, Hoover RN. Cancer and a fatiguing illness in Northern Nevada—a causal hypothesis. *Ann Epidemiol* 1998;8:245-9.
8. Gilliam AG. Epidemiologic study of an epidemic diagnosed as poliomyelitis occurring among the personnel of the Los Angeles County General Hospital during the summer of 1934. Bulletin 240. Washington, DC: U.S. Public Health Service Division of Infectious Disease. National Institutes of Health 1938;1-90.
9. Sigurdsson B, Sigurjonsson J, Sigurdsson JHJ, Thorkelsson J, Gudmondsson KR. A disease epidemic in Iceland simulating poliomyelitis. *Am J Hyg* 1950; 52: 222-38.
10. Henderson DA, Shelokov A. Epidemic neuromyasthenia, clinical syndrome? *N Eng J Med* 1959;260:757-64.
11. Briggs NC, Levine PH. A comparative review of systemic and neurological symptomatology in 12 outbreaks collectively described as chronic fatigue syndrome, epidemic neuromyasthenia and myalgic encephalomyelitis. *Clin Infect Dis* 1994;18 (Suppl 1):S32-42.
12. Levine PH, Snow PG, Ranum BA, Paul C, Homes MJ. Epidemic neuromyasthenia and chronic fatigue syndrome in West Otago, New Zealand. *Arch Intern Med* 1997;157:750-54.
13. Dilman DA. Mail and telephone surveys. New York: John Wiley and Sons, 1978;21-8.
14. Fox CM, Robinson KL, Boardley D. Cost-effectiveness of follow-up strategies in improving the response rate of mail surveys. *Industrial Marketing Management*. 1998;27:127-33.
15. Mawle AC, Nisenbaum R, Dobbins JG, et al. Seroepidemiology of chronic fatigue syndrome: a case-control study. *Clin Infect Dis* 1995;21:1386-9.
16. Buchwald D, Pearlman T, Umali J, Schmalin K, Katon W. Functional status in

patients with chronic fatigue syndrome, other fatiguing illnesses and healthy individuals. *Am J Med* 1996;101:364-70.

17. MacDonald KL, Osterholm MT, LeDell KH, et al. A case-control study to assess possible triggers and cofactors in chronic fatigue syndrome. *Am J Med* 1996; 100:548-54.

18. Cannon JG, St. Pierre BA. Gender differences in host defense mechanisms. *J Psychiatr Res* 1997;31:99-113.



**For FACULTY/PROFESSIONALS with journal subscription recommendation authority for their institutional library . . .**

If you have read a reprint or photocopy of this article, would you like to make sure that your library also subscribes to this journal? If you have the authority to recommend subscriptions to your library, we will send you a free complete (print edition) sample copy for review with your librarian.

1. Fill out the form below and make sure that you type or write out clearly both the name of the journal and your own name and address. Or send your request via e-mail to [getinfo@haworthpressinc.com](mailto:getinfo@haworthpressinc.com) including in the subject line "Sample Copy Request" and the title of this journal.
2. Make sure to include your name and complete postal mailing address as well as your institutional/agency library name in the text of your e-mail.

[Please note: we cannot mail specific journal samples, such as the issue in which a specific article appears. Sample issues are provided with the hope that you might review a possible subscription/e-subscription with your institution's librarian. There is no charge for an institution/campus-wide electronic subscription concurrent with the archival print edition subscription.]

☐ **YES!** Please send me a complimentary sample of this journal:

(please write complete journal title here—do not leave blank)

I will show this journal to our institutional or agency library for a possible subscription.

Institution/Agency Library: \_\_\_\_\_

Name: \_\_\_\_\_

Institution: \_\_\_\_\_

Address: \_\_\_\_\_

City: \_\_\_\_\_ State: \_\_\_\_\_ Zip: \_\_\_\_\_

Return to: Sample Copy Department, The Haworth Press, Inc.,  
10 Alice Street, Binghamton, NY 13904-1580